

# **Sponsor: Epigenomics AG**

**PMA: P130001**

**Molecular and Clinical Genetics Panel Meeting  
Medical Devices Advisory Committee**

March 26, 2014



# Introduction and Device Description

**Thomas Taapken, PhD**

CEO, Epigenomics

# Epi proColon<sup>®</sup>: First of a Kind Blood Screening Test for Colorectal Cancer



# Agenda and Presenters

**Introduction and  
Device Description**

**Thomas Taapken, PhD**  
CEO, Epigenomics

**Colorectal Cancer Screening  
Medical Need**

**David Johnson, MD**  
Professor of Internal Medicine and  
Chief of Division of Gastroenterology  
Eastern Virginia Medical School

**Analytical Validation  
Pivotal Clinical Trial**

**Nicholas Potter, PhD, FACMG**  
Chief Scientific Officer  
Molecular Pathology Laboratory Network (MPLN)

**Non-inferiority Trial  
Epi proColon® vs OC FIT-CHEK®**

**David Johnson, MD**

**Labeling  
Post-approval Study**

**Thomas Taapken, PhD**

**Risk-benefit Analysis  
Closing Remarks**

**David Johnson, MD**

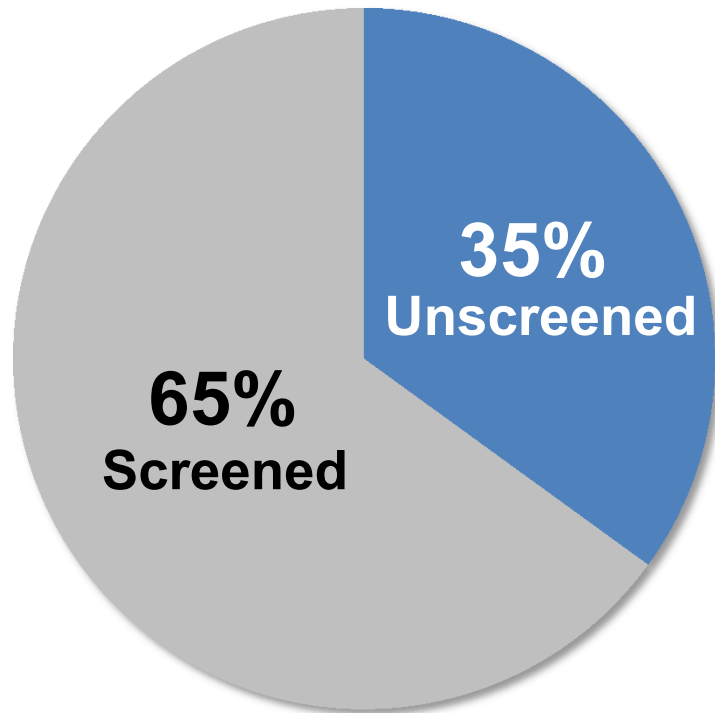
# Today's Focus: Epi proColon

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<b>Device</b>	Blood-based colorectal cancer screening test
<b>Use in practice</b>	Make screening available to average risk patients who do not utilize current standard of care screening methods
<b>Benefit once implemented</b>	Increased detection of CRC when used appropriately with colonoscopy  Additional choice for healthcare providers to help increase CRC screening participation

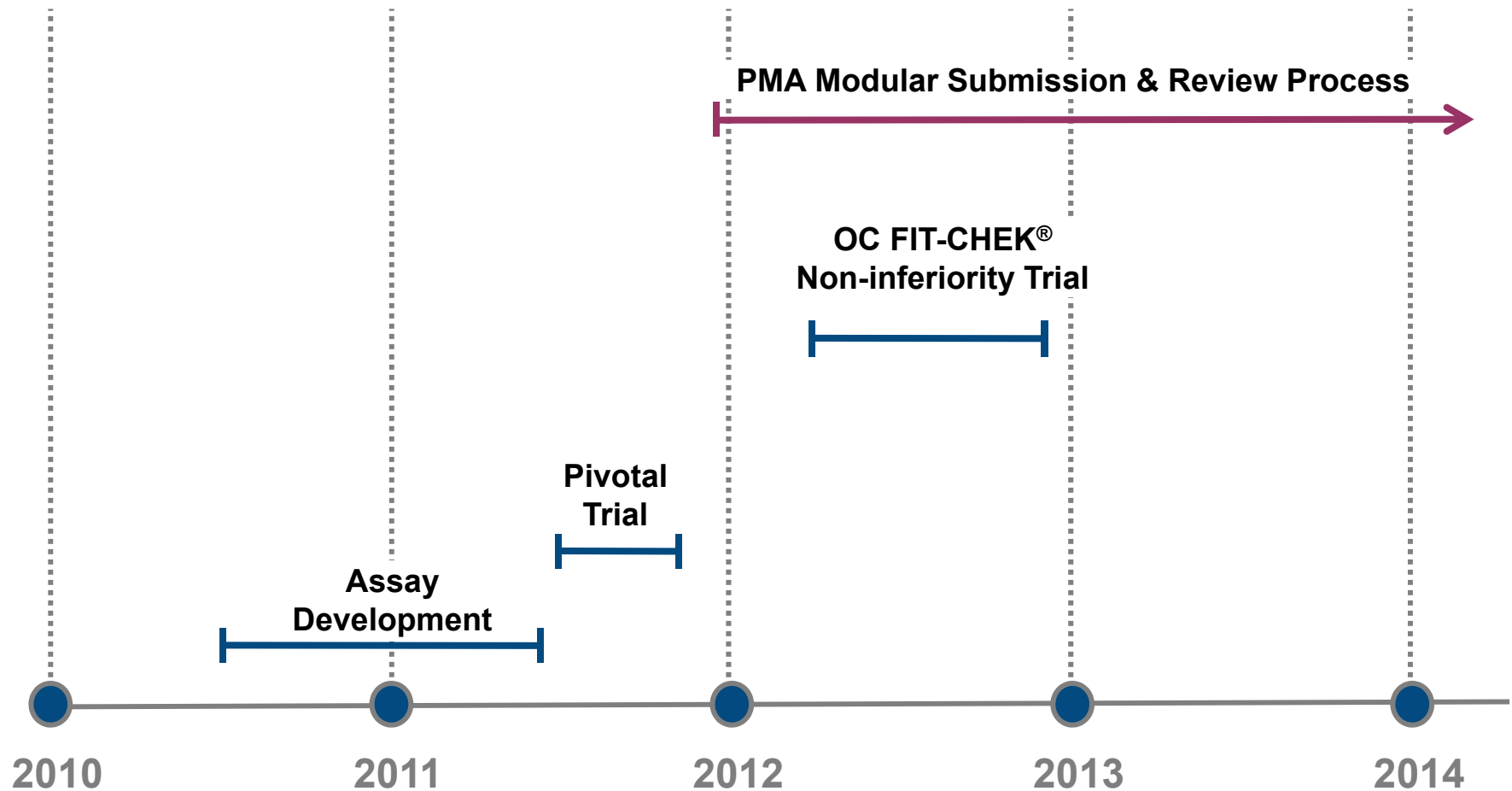
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# Colorectal Cancer Screening: Underutilized

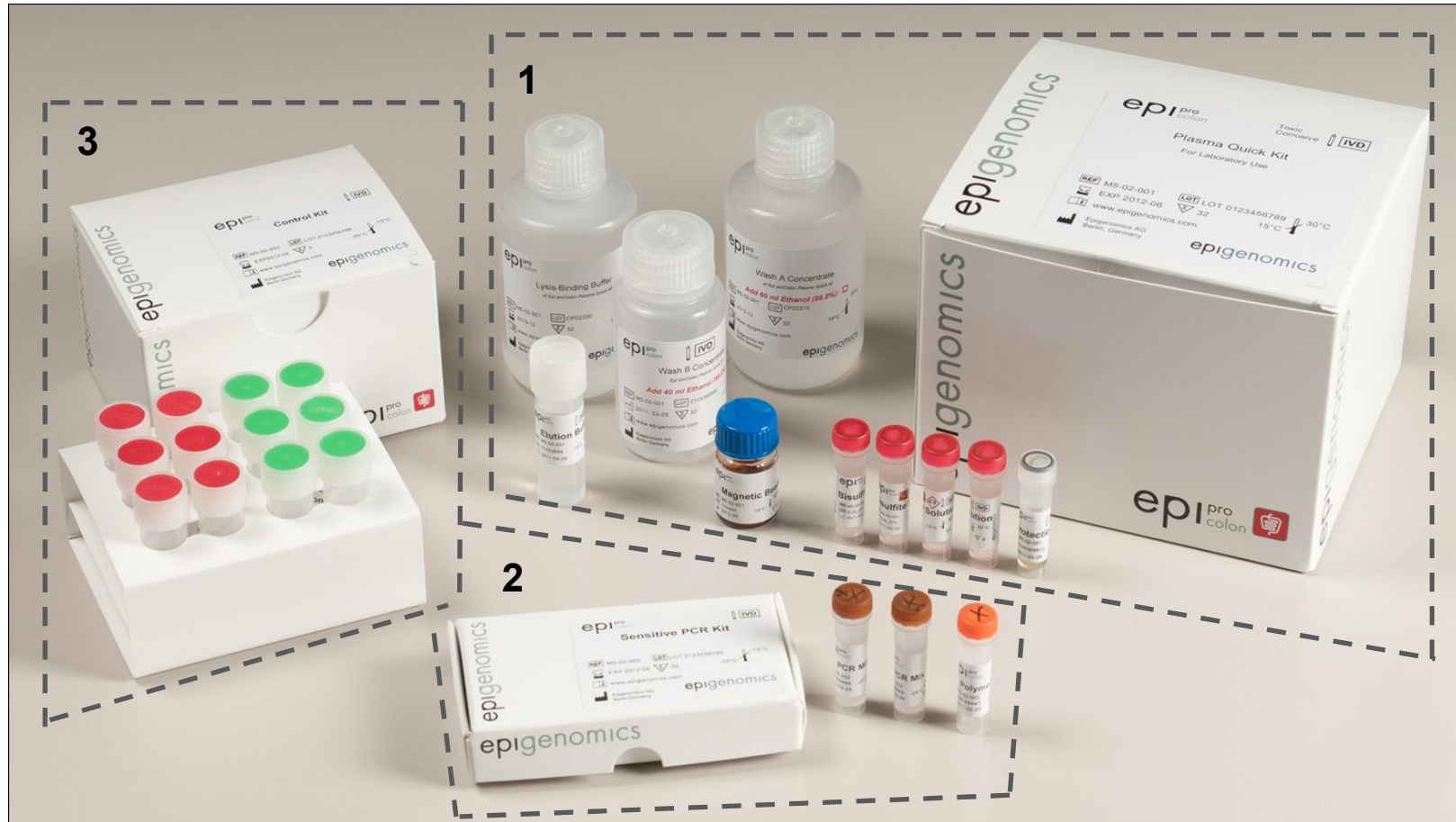


- Participation rates are low
- No screening = No detection

# Development and Regulatory Timeline



# Epi proColon: Device Description



# Epi proColon: Methylated Septin9 Biomarker

- DNA methylation:
  - Important role in colorectal cancer
  - No sequence change – cytosine modification
- Discovered by genome-wide screening
- Hypermethylated in >90% of CRC tissues
- Detectable in human plasma
- Best diagnostic accuracy among all markers tested
- Evaluated in >5,000 case/control patient samples

# Epi proColon: Methylated Septin9 Biomarker

- Septins
  - GTP binding proteins
  - Role in: vesicle trafficking, apoptosis, cytoskeletal remodeling and cell division
- Septin9 gene
  - Complex, multiple transcripts and splice variants
  - Marker sequence: gamma promoter – v2 transcript

# Two Clinical Trials

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**First**

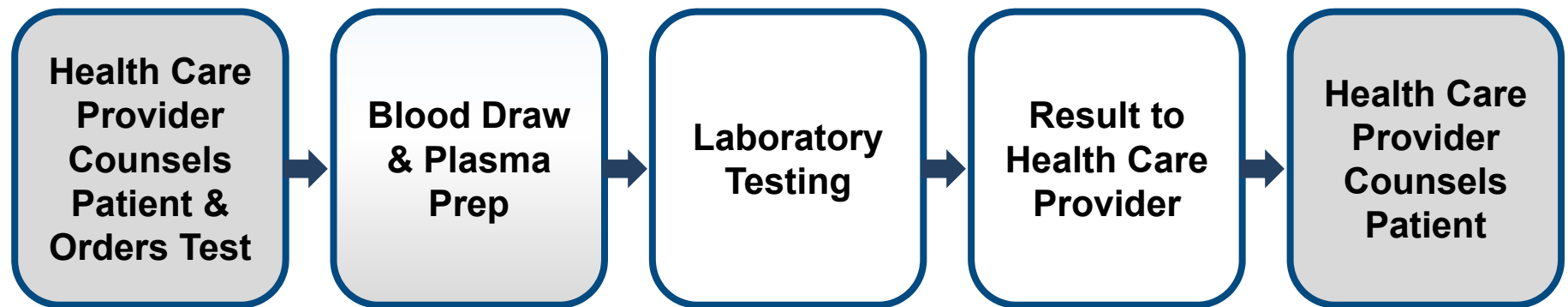
Prospective, Multicenter Pivotal Trial

**Second**

Prospective, Multicenter OC FIT-CHEK®  
Non-inferiority Comparison Trial

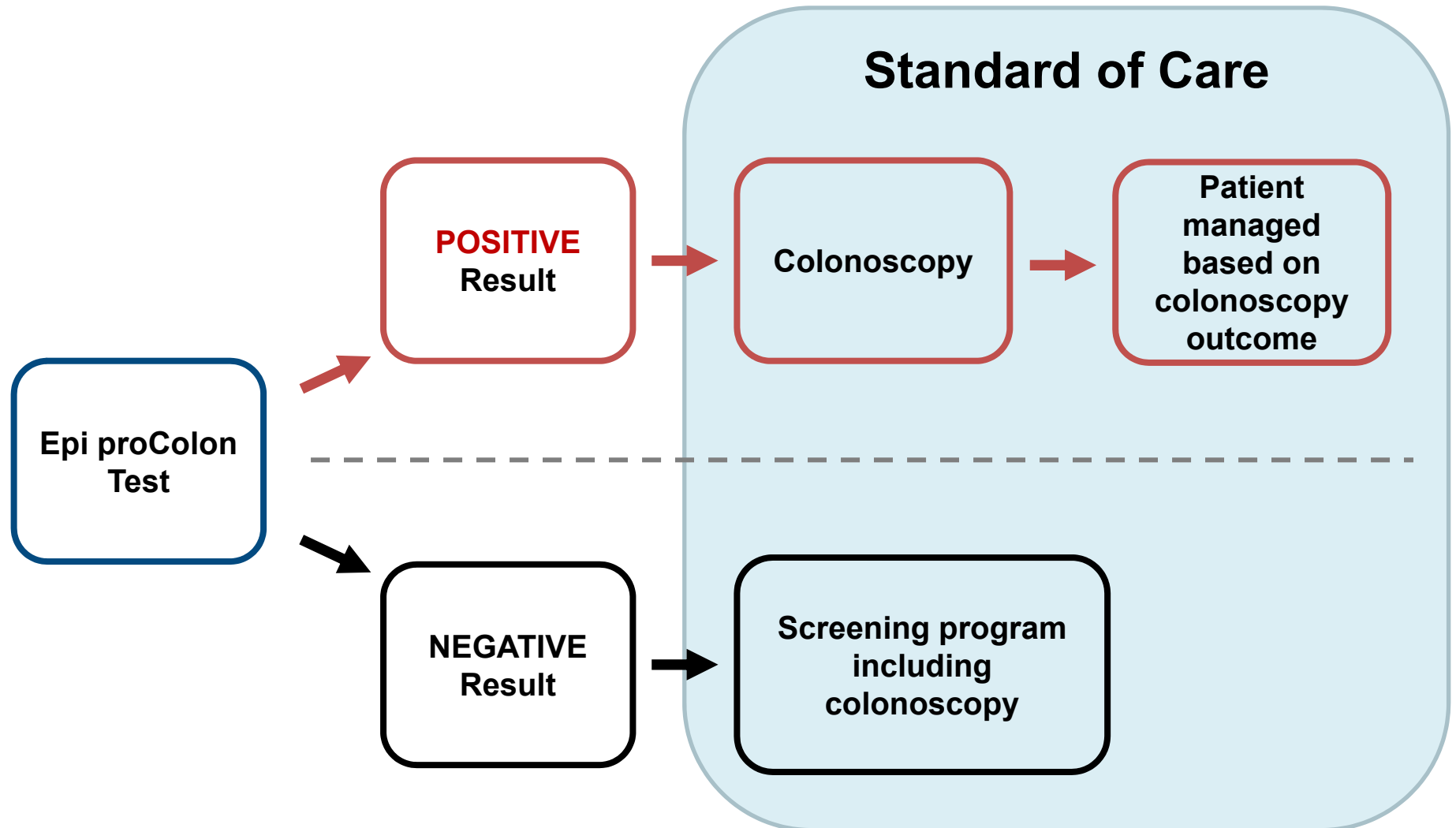
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# Epi proColon Patient Management



**Entire Process under Professional Management**

# Epi proColon Patient Management



# Proposed Intended Use

## Intended Use excerpt:

*“....The test is indicated to **screen** patients for **colorectal cancer** who are defined as **average risk** for colorectal cancer (CRC) by current CRC screening guidelines. Patients with a positive Epi proColon test result should be **referred for diagnostic colonoscopy**.*

*Men and women 50 to 85 years of age were included in the Epi proColon clinical trial. The Epi proColon test results, together with the physician's assessment of history, other risk factors, and professional guidelines, may be used to guide patient management. ...”*

## Proposed Warnings excerpt:

*“...Epi proColon test is **not intended to replace** colorectal screening by **colonoscopy**...”*

# Discussion Points

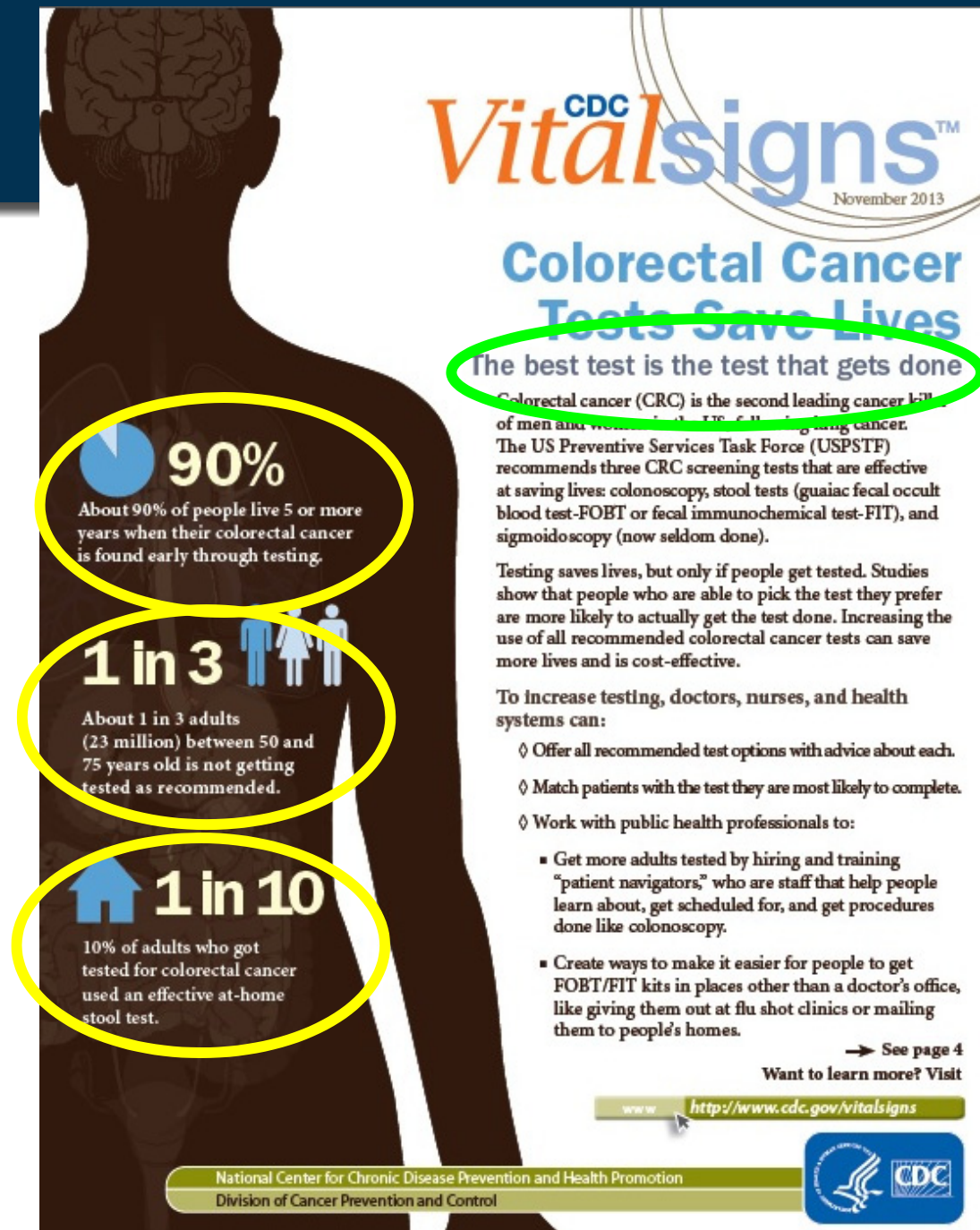
- The ability of a simple blood-based PCR test to identify a treatable disease
- Medical need and impact of the blood-based Epi proColon test for CRC screening
- Two major prospective clinical trials providing evidence for the safety and effectiveness of Epi proColon
- Recommendations for use of the test to complement current screening practice

# Colorectal Cancer Screening and Medical Need

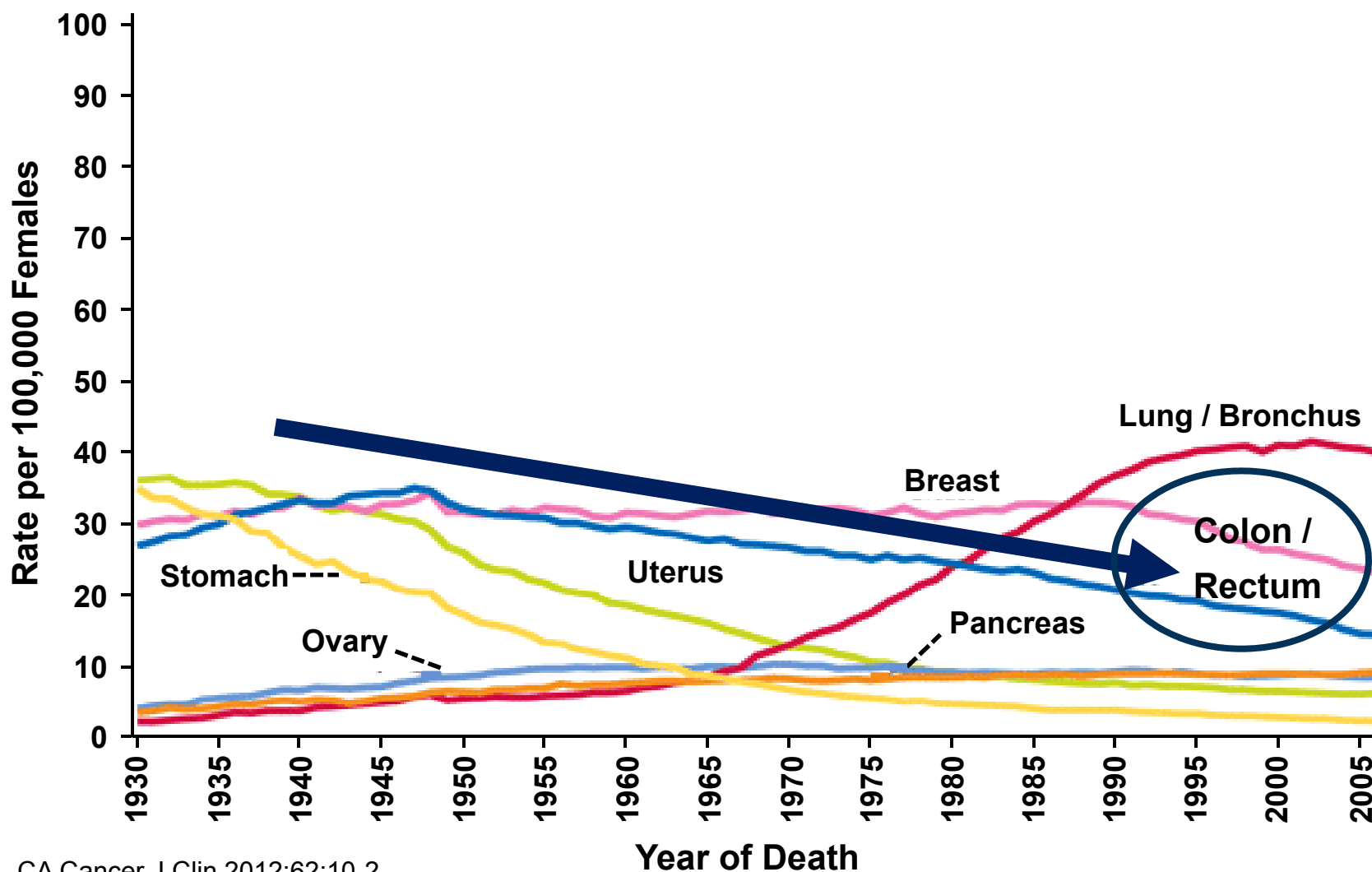
**David Johnson, MD MACG FASGE FACP**

Professor of Internal Medicine  
Chief of Division of Gastroenterology  
Eastern Virginia Medical School  
Norfolk VA

# CRC Screening



# U.S. Cancer Statistics 2012



CA Cancer J Clin 2012;62:10-2.

## Estimated New Cases

# U.S. Cancer Statistics 2012

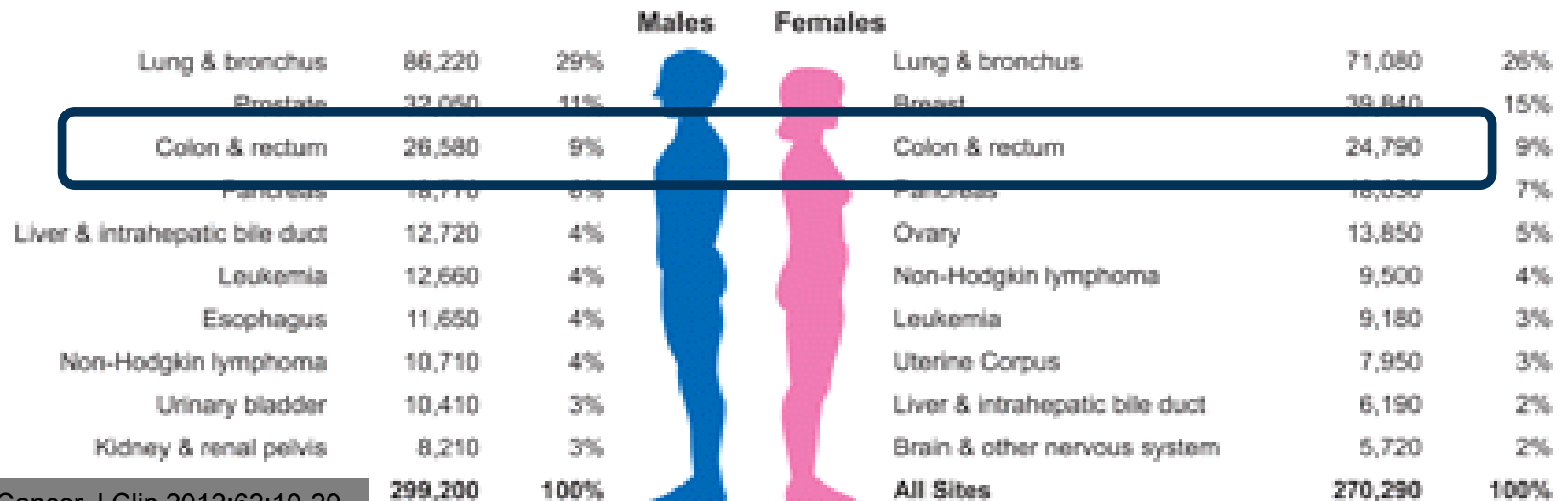


## 2012 Estimates

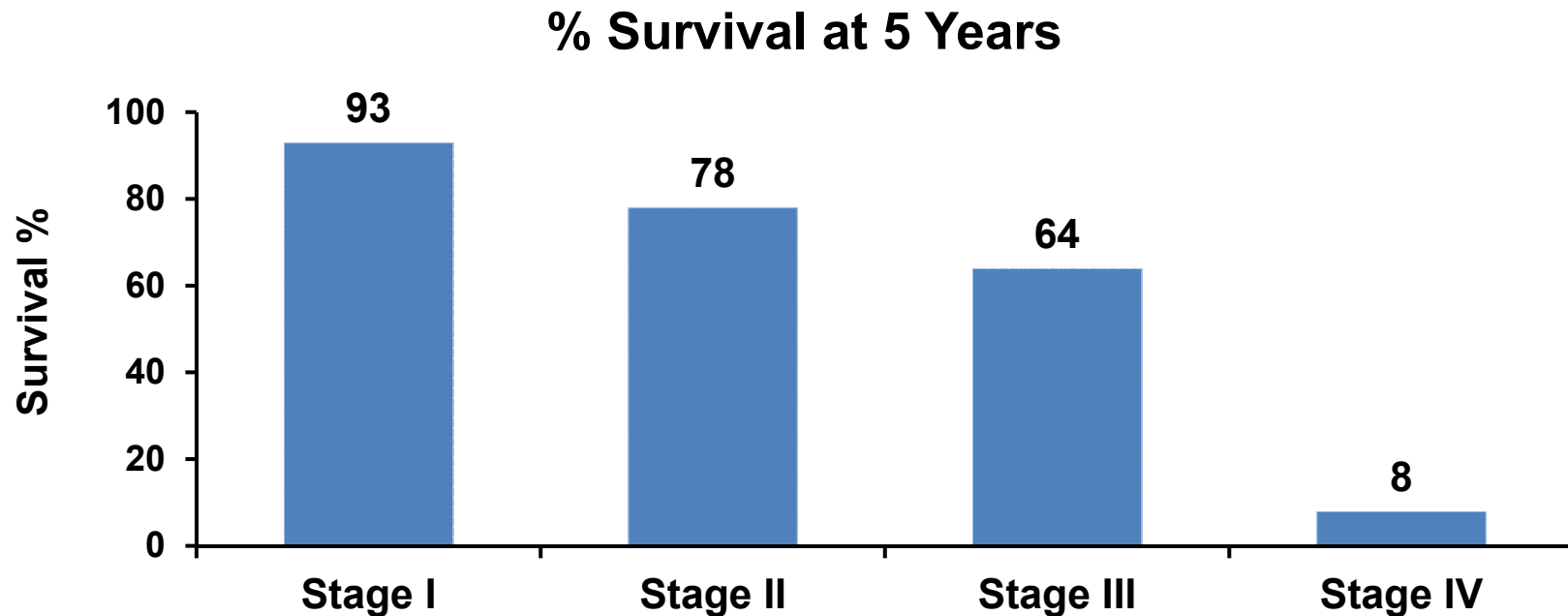
CRC New Cases: 142,570

CRC Deaths: 51,370

## Estimated Deaths



# Colorectal Cancer: Treatable Disease



- Treatable disease if detected early
- Late stage therapies improving

Colon Cancer Survival Rates with the New American Joint Committee on Cancer Sixth Edition Staging." J Nat Can Institute 2004 96:1420-1425.

# CRC Screening Methods

- Fecal Blood Test
  - Fecal occult blood (FOBT)
  - Immunochemical FOBT (FIT)
- Stool DNA
- Colonoscopy
- Flexible Sigmoidoscopy
- CT Colonography
- Barium Enema

# Most Common CRC Screening Methods

- Fecal Occult Blood Test – (FOBT / FIT)
- Colonoscopy

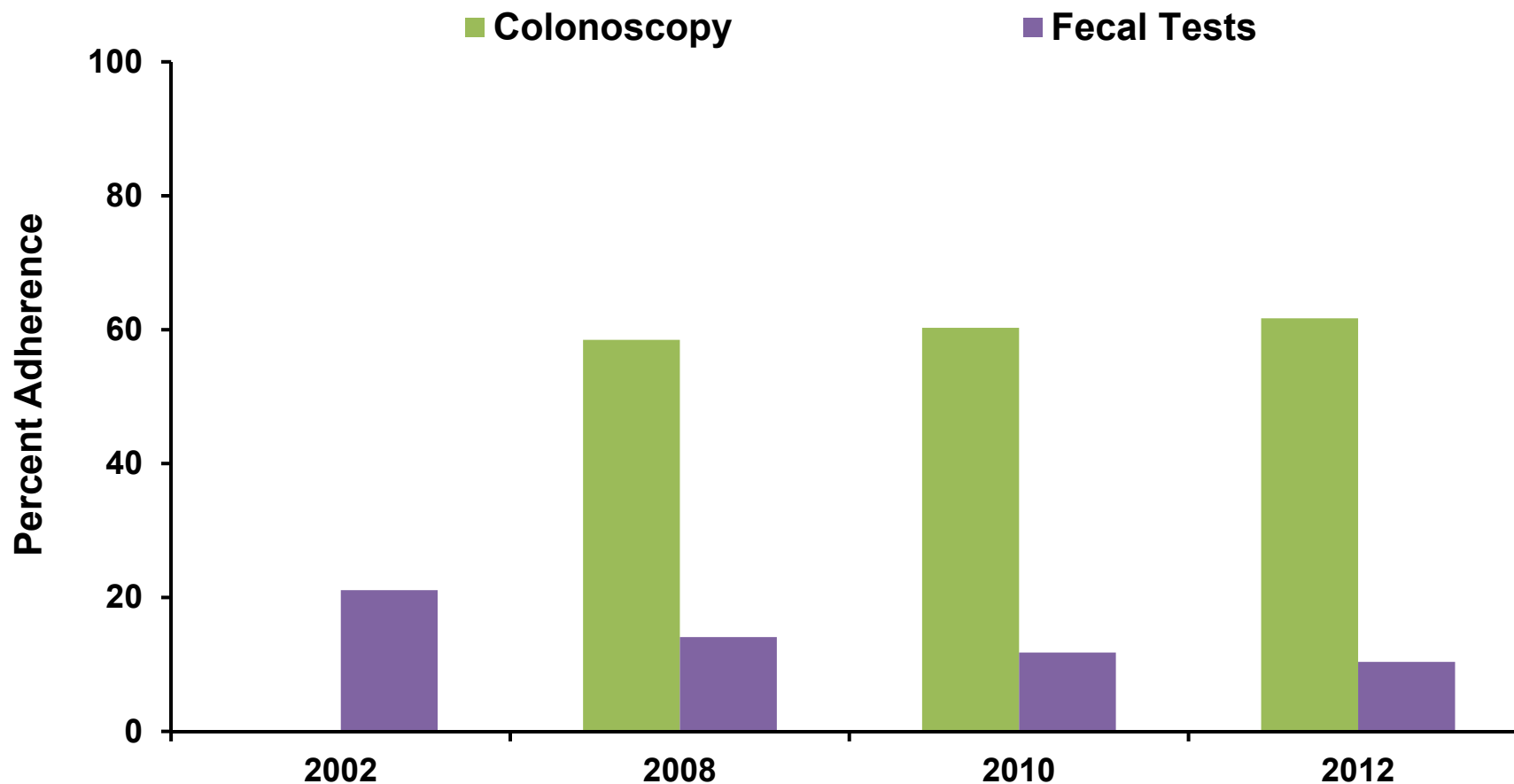
**Reference standard other methods measured**  
**Standard of care for screening**

# Colon Cancer Screening Guidelines

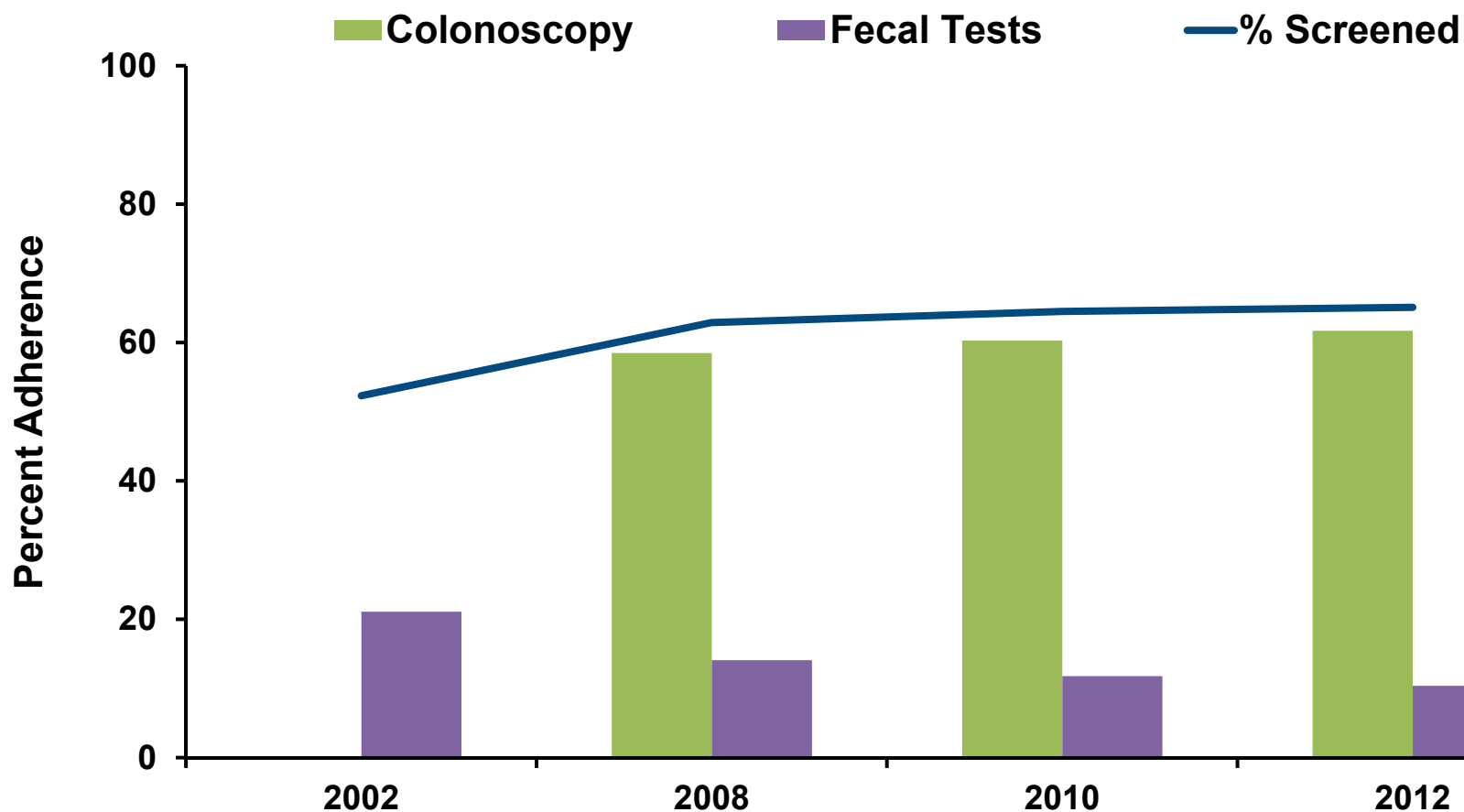
Testing Method	American Cancer Society / Multi Society Task Force Age 50 and older	United States Preventive Services Task Force, Ages 50-75
FOBT	Yearly	Yearly
FIT	Yearly	Yearly
Stool DNA	Interval Uncertain	Not Recommended
Sigmoidoscopy	Every 5 Years	Every 5 years
<b>Colonoscopy</b>	<b>Every 10 Years</b>	<b>Every 10 Years</b>
CT Colonography	Every 10 Years	Not Recommended

**Guidelines recommend colonoscopy as preferred option**

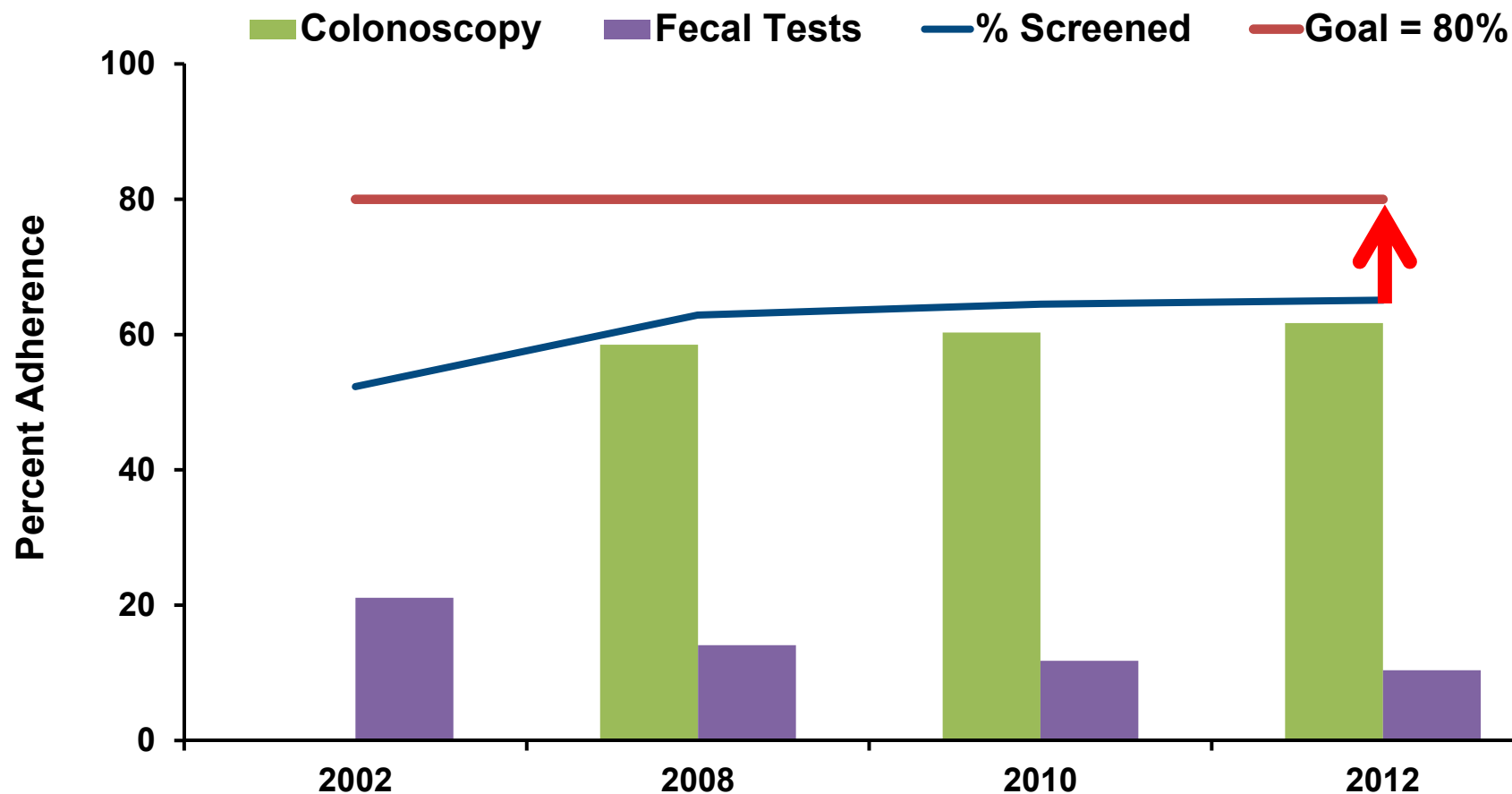
# CRC Screening Rates Remain Sub-Optimal



# CRC Screening: Rates Remain Sub-Optimal



# CRC Screening: Rates Remain Sub-Optimal



American Cancer Society Strategic Progress Report, 2013; CDC, 2014; Healthy People.gov; CDC BRFSS, 2008-2013.

Vital Signs: Colorectal Cancer Screening BRFSS Documents 2013, 2012, 2011, 2010

# CRC Screening: Closing the Gap and Saving Lives

- Survival requires detection
- Detection requires participation
- Pathways to participation

# CRC Screening: Improving Screening Participation

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<b>Choice*</b>	Increases participation
<b>Preference</b>	Adding tests that people are willing to do
<b>Innovation</b>	Providing tests to reach the unscreened

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**Closing the screening gap!**

\*Inadomi et al. Arch Intern Med. 2012; 172 (7): 575-82.

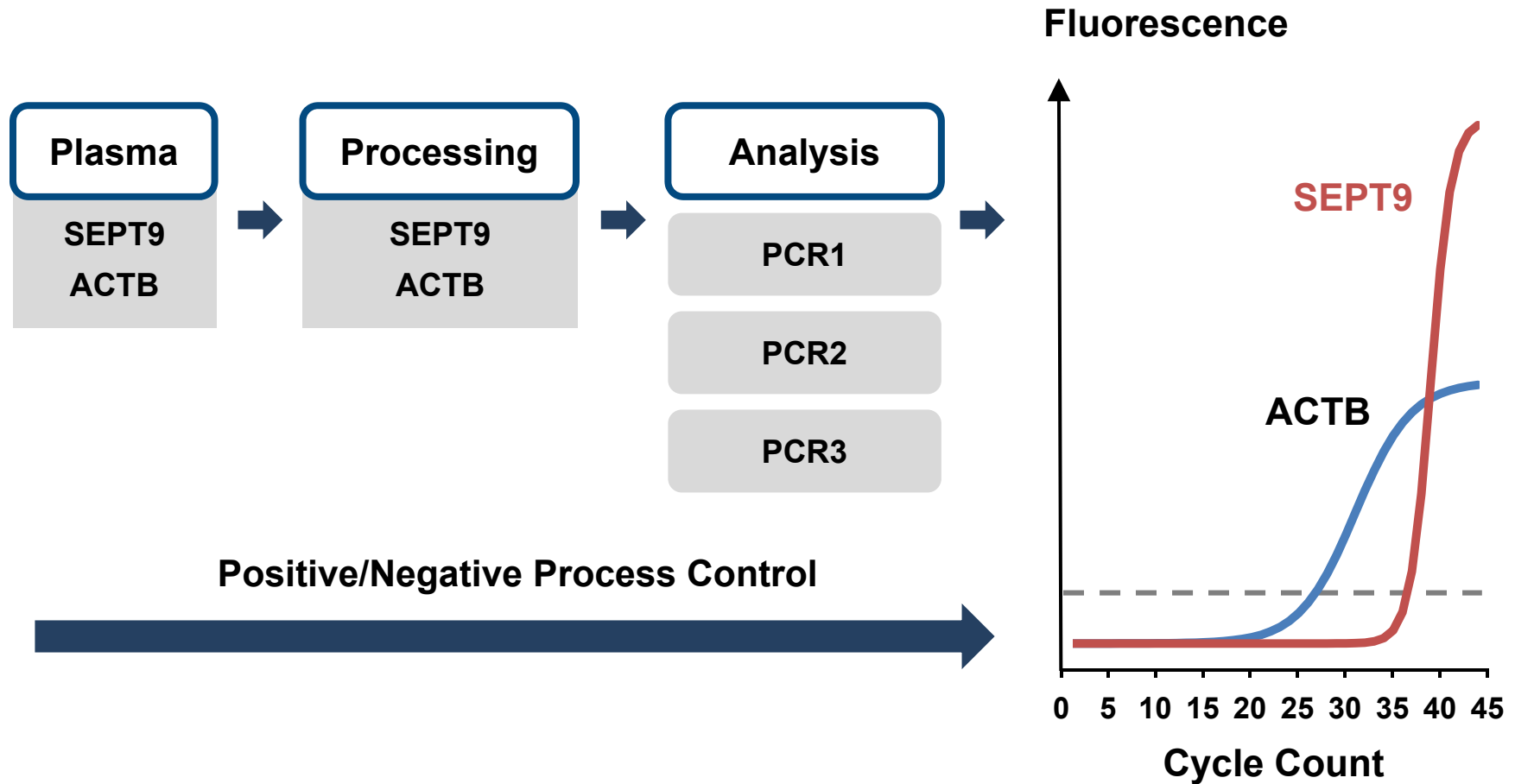
# Analytical Validation

**Nicholas Potter, PhD, FACMG**

Chief Scientific Officer

Molecular Pathology Laboratory Network (MPLN)

# Epi proColon: Laboratory Integration and Workflow



# Analytical Validation

- Analytical Sensitivity / Limit of Detection (LoD)
  - 95% LoD = 4.7 pg/mL (CI 2.5-9.0)
  - One genome equivalent per mL
- Precision and Reproducibility
  - 11 CRC pools: 98% replicates tested positive
  - 3 healthy pools: 75% replicates tested negative
- Analytical Specificity / Cross Reactivity
  - *In silico* analysis: no cross reactivity
  - Sequencing: Epi proColon detects only methylated Septin9 target

# Analytical Validation

- Interfering Substances
  - No interference – 10 common substances
  - False positive results reported at intentionally elevated concentrations of sperm DNA, albumin and red blood cells
- Robustness
  - 20 failure modes: assay performed correctly or controls indicated failure
  - Blood handling: no significant effects on test results for all testing conditions

**Epi proColon is a robust test that generates accurate results**

# Pivotal Clinical Trial

**Nicholas Potter, PhD, FACMG**

# Pivotal Trial: Objectives/Design

<b>Objectives</b>	<p><b><u>Primary</u></b>: Detection of CRC by Epi proColon, compared to detection of CRC by colonoscopy, followed by histological confirmation</p> <p><b><u>Secondary</u></b>: Evaluate test positivity in clinically defined subgroups</p>
<b>Design</b>	Multicenter prospective clinical specimen collection; blinded multicenter testing in three independent laboratories
<b>Subjects</b>	Archived specimens from PRESEPT trial
<b>Goals</b>	Target sensitivity: 65% Target specificity: 85%
<b>Analysis</b>	Comparison of point estimates of clinical performance to target values

# Pivotal Trial: Clinical Subgroup Definitions

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<b>CRC</b>	Colorectal cancers, confirmed by colonoscopy / pathology (stages I-IV)
<b>AA</b>	Advanced adenomas: adenomatous polyp(s) $\geq 10$ mm and adenomas with villous component or high grade dysplasia (HGD)
<b>SP</b>	Small polyps: non-advanced adenoma and polyps $< 10$ mm, no villous component or HGD
<b>NED</b>	No evidence of disease: no evidence of any above

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# Pivotal Trial: Archived Plasma from PRESEPT

PRESEPT Trial Sample Collection (NCT00855348):

- 7941 enrolled in clinical trial
- 32 clinical sites: 22 US, 10 Germany
- 6857 plasma samples from trial subjects available for pivotal trial
- Colonoscopy was the reference standard

# Pivotal Trial: Archived Plasma from PRESEPT

## Inclusion Criteria:

- $\geq$  Age 50, screening guideline-eligible, at colonoscopy
- First colonoscopy in lifetime

## Capable of:

- Informed consent process
- Providing health history
- Blood draw prior to start of bowel prep for colonoscopy

# Pivotal Trial: Archived Plasma from PRESEPT

## Exclusion Criteria

- Bleeding
- Hematochezia, or known iron deficiency anemia
- Previous history of polyps or CRC
- High risk for CRC
  - Two or more, 1<sup>o</sup> relatives with CRC
  - One or more, 1<sup>o</sup> relative(s) <50 years with CRC
  - Known hereditary nonpolyposis colorectal cancer (HNPCC) or familial adenomatous polyposis (FAP)

# Pivotal Trial: PRESEPT Demographics

Demographic Factor	Value	PRESEPT Sample Collection
Gender	Male	45%
	Female	55%
Age	50–59	46%
	60–69	42%
	>69	12%
Race/Ethnicity	Caucasian	85%
	African-American	10%
	Others	5%
Country	U.S.A	75%
	Germany	25%

# Pivotal Trial: Plasma Samples Available

Subjects	CRC	AA	SP	NED	Total
Enrolled in PRESEPT	-	-	-	-	7941
<b>Available for pivotal trial</b>	<b>50</b>	<b>653</b>	<b>2369</b>	<b>3785</b>	<b>6857</b>

- Main reasons for subjects unavailable for pivotal trial
  - Failed inclusion/exclusion criteria
  - Incomplete data (colonoscopy)
  - Insufficient sample amount

# Pivotal Trial: Trial Design

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CRC

Tested all samples

AA

Tested all samples

NED and SP

Subset testing

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# Pivotal Trial: NED and SP Subsets

- Highly precise specificity estimate (95% CI  $\pm 2\%$ )
- Sampling Method: computer-generated stratified random sampling
- Sampling Criteria:
  - Age profile to match US Census data
  - Equal gender representation
  - Representation of ethnic minorities to allow for subgroup analysis

# Pivotal Trial: Tested Samples

Subjects	CRC	AA	SP	NED	Total
Enrolled in PRESEPT	-	-	-	-	7941
Available for pivotal trial	50	653	2369	3785	6857
<b>Pivotal trial samples</b>	<b>50</b>	<b>650</b>	<b>454</b>	<b>469</b>	<b>1623</b>

# Pivotal Trial: Testing

- Samples randomized and identities masked
- Tested in 3 independent US laboratories
- Testing completed and final results reported by all sites prior to analysis
- Unmasking, analysis and reporting by Epigenomics as per clinical trial protocol

# Pivotal Trial: Valid Results

Subjects	CRC	AA	SP	NED	Total
Enrolled in PRESEPT	-	-	-	-	7941
Available for pivotal trial	50	653	2369	3785	6857
Pivotal trial samples	50	650	454	469	1623
<b>Valid results</b>	<b>44</b>	<b>621</b>	<b>435</b>	<b>444</b>	<b>1544</b>

# Pivotal Trial Results: Sensitivity and Specificity

Parameter	% Point Estimate (CI 95%)	N/Total
Sensitivity (CRC)	68.2% (53.4 – 80.0%)	30/44
Observed specificity (Non-CRC)	78.8% (76.7 – 80.8%)	1182/1500

# Pivotal Trial Results: Sensitivity and Specificity

Parameter	% Point Estimate (CI 95%)	N/Total
Sensitivity (CRC)	68.2% (53.4 – 80.0%)	30/44
Observed specificity (Non-CRC)	78.8% (76.7 – 80.8%)	1182/1500
Specificity adjusted to US census population	79.1% (77.0 – 81.4%)	N/A
Specificity adjusted to PRESEPT patient cohort	80.0% (77.9 – 82.1%)	N/A

# Pivotal Trial: Sensitivity

- Sensitivity target of 65% met (68%)
  - Sensitivity endpoint selected based on results with Septin9 prototype tests
  - Lower bound of CI <65%
  - Primary objective was formulated as a point estimate criterion
  - Internal risk-benefit analysis with input from external medical advisors:
    - Blood test with demonstrated performance justifies decision to proceed because of potential to increase participation in CRC screening

# Pivotal Trial: Specificity

- Specificity target of 85% not met (80%)
  - Specificity endpoint selected based on results with Septin9 prototype tests
  - Internal risk-benefit analysis with input from external medical advisors:
    - Blood test with demonstrated performance justifies decision to proceed because of potential to increase participation in CRC screening and direct patients to guideline recommended screening (colonoscopy)
    - No safety concerns raised

# Pivotal Trial: Secondary Objective Test Positivity in Non-CRC Subjects

Clinical Group	Point Estimate (CI 95%)	N/Total
No Evidence of Disease (NED)	21.8% (18.3 – 25.9%)	97/444
Small Polyps (SP)	20.0% (16.5 – 24.0%)	87/435
Advanced Adenomas (AA)	21.6% (18.5 – 25.0%)	134/621
Total Non-CRC	21.2% (19.2 – 23.3%)	318/1500

# Pivotal Trial: Additional Analysis

## Test Positivity by Cancer Stage

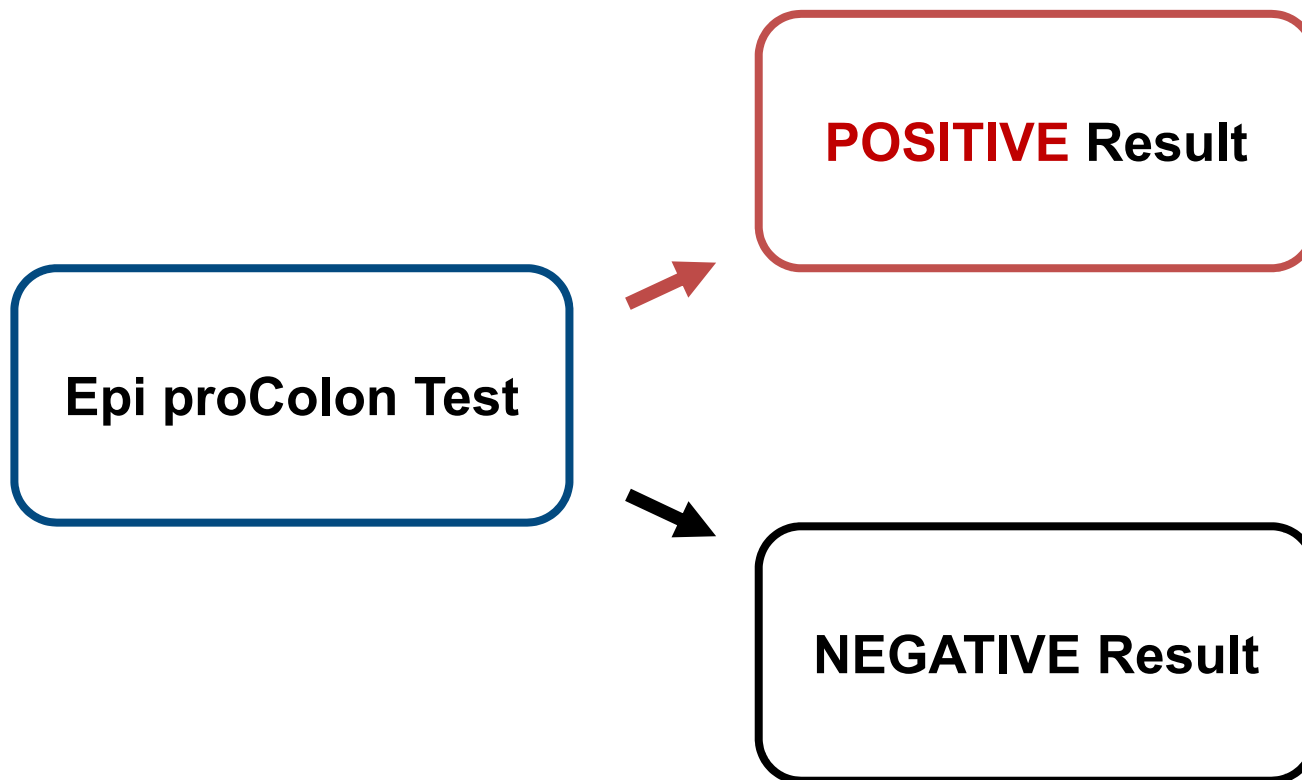
CRC Stage	% Point Estimate (CI 95%)	N/Total
Stage I	41% (22 – 64%)	7/17
Stage II	83% (55 – 95%)	10/12
Stage III	80% (49 – 94%)	8/10
Stage IV	100% (57 – 100%)	5/5
Total Cancers	68% (53 – 80%)	30/44

# Pivotal Trial: Additional Analysis

## Test Positivity by CRC Location

Location	% Point Estimate (CI 95%)	N/Total
Proximal Colon	70% (52 – 83%)	21/30
Distal Colon	64% (39 – 84%)	9/14

# Pivotal Trial: Medical Perspective



# Pivotal Trial: Diagnostic Likelihood Ratios

Epi proColon Test Result	Parameter	Point Estimate (95% CI)
Positive	Positive Diagnostic Likelihood Ratio (pDLR)	3.41 (2.72 – 4.27)
Negative	Negative Diagnostic Likelihood Ratio (nDLR)	0.40 (0.26 – 0.61)

pDLR = sensitivity / (1 – specificity)   nDLR = (1 – sensitivity) / specificity

- If Epi proColon positive, patient is 3.4 times more likely to have colorectal cancer
- If Epi proColon negative, patient is 2.5 (=1/0.4) times less likely to have colorectal cancer

# Performance Measures in Age Subgroups

Age Group	Sensitivity	Specificity	pDLR	nDLR
49-59	0.75	0.84	4.58	0.3
60-69	0.67	0.76	2.83	0.44
>69	0.69	0.74	2.63	0.42

- Decreasing specificity with age
- Patients over age 69:
  - Epi proColon positive, patient 2.6 x more likely to have CRC
  - Epi proColon negative, patient 2.4 ( $=1/0.42$ ) x less likely to have CRC

# Performance Measures in Ethnic Subgroups

Ethnic Group	Sensitivity	Specificity	pDLR	nDLR
African-American	0.67	0.73	2.46	0.46
Caucasian	0.69	0.80	3.42	0.39
Other	0.5	0.82	2.76	0.61

- Reduced specificity in African Americans
- In African American subgroup:
  - Epi proColon positive, patient 2.5 x more likely to have CRC
  - Epi proColon negative, patient 2.2 ( $=1/0.46$ ) x less likely to have CRC

# Pivotal Trial: Summary and Conclusion

- **Sensitivity:**       **68%** (95% CI 53 – 80%)
- **Specificity:**       **80%** (95% CI 78 – 82%)
- No significant detection in AA, SP
  - Epi proColon not designed for adenoma detection
- Detects CRC at all stages
  - Combined sensitivity for treatable CRC stages I-III was 64.1%
- Equal detection in proximal / distal colon
- CRC detection not influenced by ethnicity or age
- False positive rate increased with increasing age and in African American subjects
- Based on DLRs, Epi proColon provides valuable information for patient of all subgroups analyzed

# **Non-inferiority Trial Epi proColon<sup>®</sup> vs OC FIT-CHEK<sup>®</sup>**

**David Johnson, MD MACG FASGE FACP**

Professor of Internal Medicine  
Chief of Gastroenterology  
Eastern Virginia Medical School  
Norfolk VA

# Non-inferiority Trial: Epi proColon vs OC FIT-CHEK

- Rationale: support the data from pivotal trial
- Compare performance with FIT
  - Guideline recommended CRC screening method
- Selected OC FIT-CHEK
  - A top performing most widely used commercial FIT

# Non-inferiority Trial: Objectives/Design

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<b>Objective</b>	Demonstration of non-inferiority of clinical performance of Epi proColon to OC FIT-CHEK
<b>Design</b>	Multicenter, prospective comparison of Epi proColon and OC FIT-CHEK to colonoscopy as a reference standard
<b>Subjects</b>	100 screen-detected CRC patients 200 average risk, screening eligible subjects
<b>Goals</b>	Non-inferiority for sensitivity, specificity Margins: 10% for sensitivity, 20% for specificity
<b>Analysis</b>	Two-sided 95% CI for sensitivity, specificity differences compared to non-inferiority margins

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# Non-inferiority Trial: Study Design

- 61 US clinical sites
- Group A: Post-screening colonoscopy
  - Detected by screening colonoscopy
  - High suspicion of or has CRC
  - Blood and stool collected > 9 days post colonoscopy
- Group B: Before screening colonoscopy, prospective
  - Blood and stool collected prior to bowel preparation

Blinded, independent laboratory testing

# Non-inferiority Trial: Inclusion and Exclusion

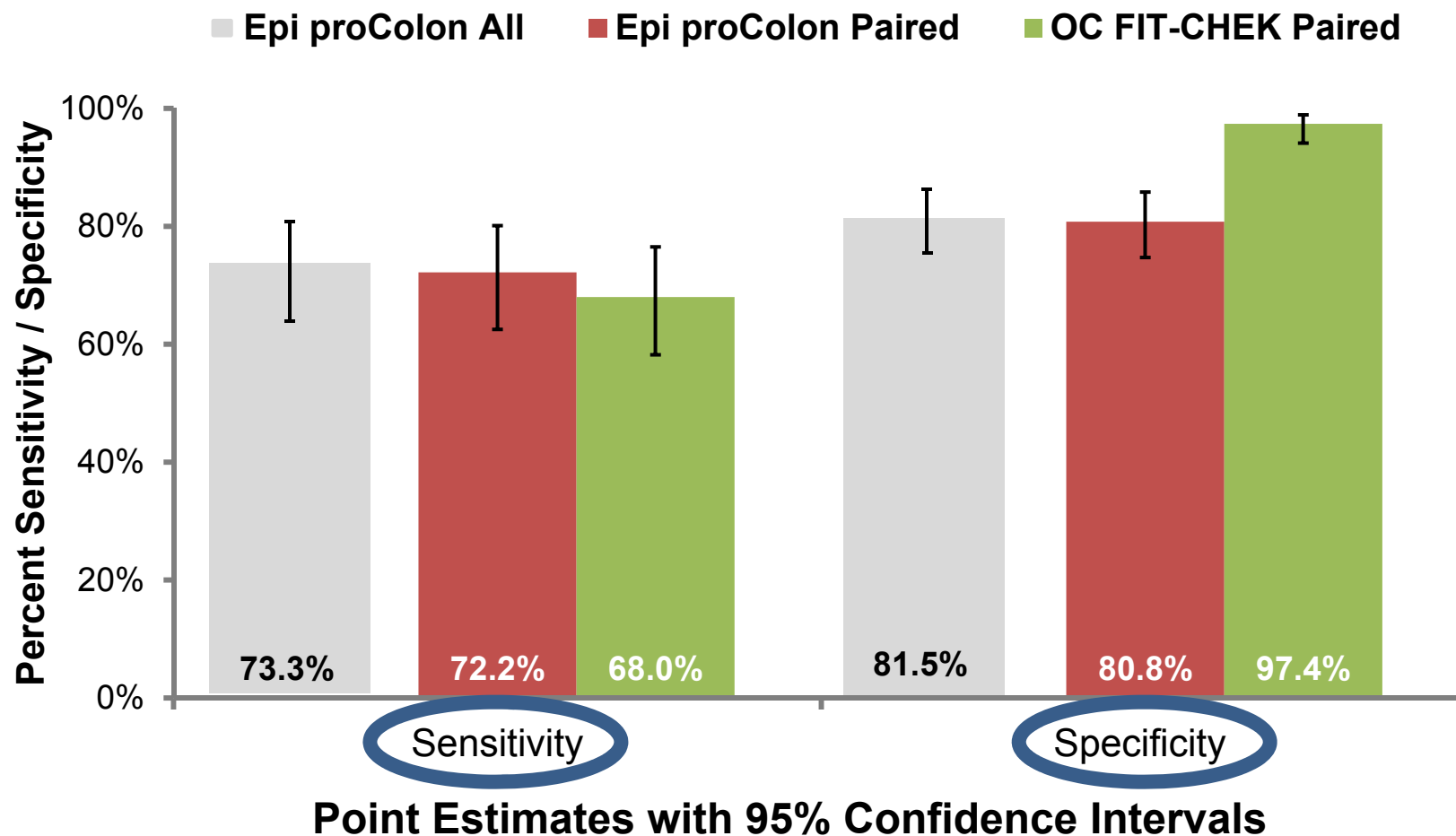
- Criteria similar to Pivotal Trial
- Group A specific additional requirement:
  - Colonoscopic diagnosis or
    - Strong clinical suspicion of colorectal carcinoma (CRC)
  - Confirmed CRC diagnosis post-surgery
    - Complete pathology report

# Non-inferiority Trial: Subjects Tested

- 290 subjects with paired plasma and stool specimens
- 11 additional subjects - plasma only
- Demographics balanced across age, gender, ethnicity

Clinical Group	Value	Plasma Samples	Stool Samples
Cancer	CRC	101	97
Non Cancer	AA	29	27
	SP	77	75
	NED	94	91
Total		301	290

# Non-Inferiority Trial: Primary Endpoint Results



# Interpretation of Primary Study Objectives

- Sensitivity: Non-inferiority Objective Met
  - Point estimate of -4.2% for difference in sensitivity within predetermined non inferiority margin of 10%
  - Upper bound of CI of 8.1% inside of 10% margin
  
- Specificity: Non-inferiority Objective Not Met
  - Point estimate of 16.6% for difference in specificity within predetermined non inferiority margin of 20%
  - Upper bound of CI of 22.9% outside of 20% margin

# Non-inferiority Trial: Diagnostic Likelihood Ratios

Parameter	Epi proColon*	OC FIT-CHEK*
Positive DLR	3.96 (2.89-5.42)	26.26 (10.94-63.05)
Negative DLR	0.33 (0.24-0.46)	0.33 (0.24-0.44)

\*Estimate (95% CI)

# Non-inferiority Trial: CRC Matched Sample Results

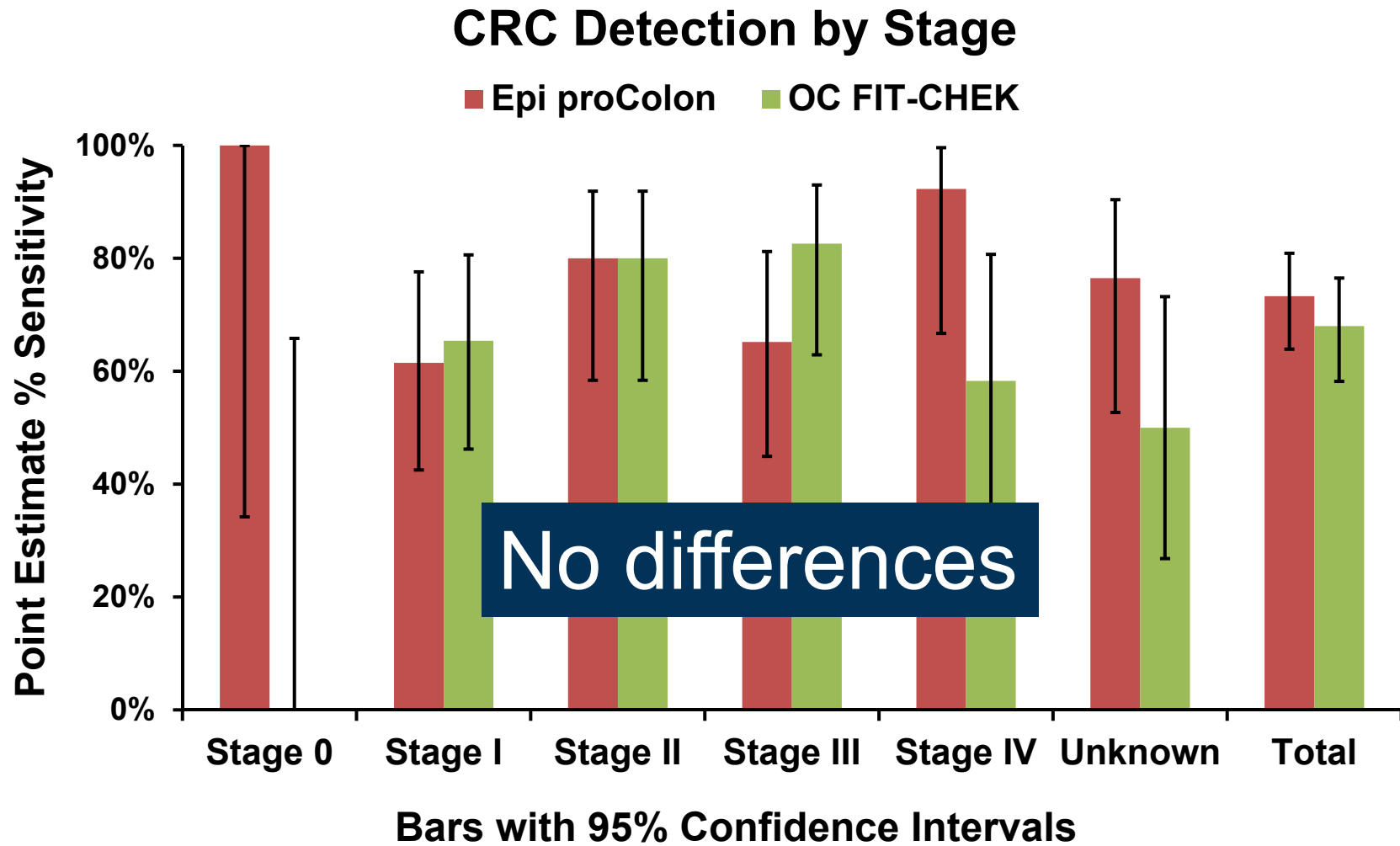
	Epi proColon Positive	Epi proColon Negative
OC FIT-CHEK Positive	50	<b>16</b>
OC FIT-CHEK Negative	<b>20</b>	11

# Non-inferiority Trial: Sensitivity by Tumor Location

Location	Epi proColon		OC FIT-CHEK	
	Point Estimate (95% CI)	N / Total	Point Estimate (95% CI)	N / Total
Proximal Colon	<b>73.1%</b> (59.7 – 83.2%)	38 / 52	<b>70.6%</b> (57.0 – 81.3%)	36 / 51
Distal Colon	<b>75.0%</b> (58.9 – 86.2%)	27 / 36	<b>69.4%</b> (55.1 – 82.0%)	25 / 36

**No differences**

# Non-inferiority Trial: Sensitivity by Tumor Stage



# Non-inferiority Trial: Summary and Conclusions

## **Epi proColon:**

- Sensitivity statistically non-inferior to OC FIT-CHEK
- Specificity not statistically non-inferior to OC FIT-CHEK
- Clinical performance consistent with pivotal trial results
  - Sensitivity: 73.3% vs 68.2% (pivotal trial)
  - Specificity: 81.5% vs 80.0% (pivotal trial)

# Non-Inferiority Trial: Summary and Conclusions

## **Both tests:**

- Performed equally well to confirm absence of CRC
  - Based on  $nDLR = 0.33$
- Identified similar numbers of CRC patients
  - Though not necessarily the same individuals
- Consideration of joint testing with OC FIT-CHEK
  - Defer to screening guidelines
- Comparable CRC detection at all stages
- Showed equivalent sensitivity for CRC detection
  - Proximal/distal colon

# Labeling

**Thomas Taapken, PhD**

CEO, Epigenomics

# Labeling: Intended Use

Key Intended Use Statements	Rationale
Screening patients at average risk for colorectal cancer	Public Health Issue – 35% of US population not screened Blood test can increase screening participation Evidence supports proposed intended use
A positive test result should be referred for diagnostic colonoscopy	Screening test is not diagnostic Requires confirmation by standard of care method, colonoscopy
Test result is used in conjunction with physician's assessment of patient history and other risk factors	Patient management should be by health care providers All results should be interpreted in the context of patient history

# Labeling: Warnings

Key Warnings Statements	Rationale
Not intended to replace colorectal cancer screening by colonoscopy	As per screening guidelines, colonoscopy remains the standard of care  Colonoscopy is the initial required step in treatment
Positive results are not confirmatory evidence for the presence of colorectal cancer	Data demonstrates need for follow-up diagnostic colonoscopy
Negative results do not guarantee absence of cancer and patients with a negative result counseled to continue in screening programs	Epi proColon is not positive in all patients with CRC  CRCs may develop during any screening program interval

# Labeling: Limitations

Key Limitations Statements	Rationale
Alternative for patients who are defined as average risk for colorectal cancer by current screening guidelines, and who are unwilling, unable or do not undergo screening by other recommended screening methods	To limit use of the test to the non-adherent population To prevent test use in already compliant population
There is insufficient evidence to report programmatic sensitivity of the Epi proColon test over an established period of time	Data is not available at this time

# Supporting Documentation

- In addition to the Intended Use Statement, Warnings and Limitations, Epigenomics has developed a comprehensive set of materials for health care professionals, laboratories and patients to insure appropriate use of the product according to its instructions for use

# Post-Approval Study

# Post-Approval Study: Overview

- Epigenomics has considered a clinical study designed to obtain programmatic performance data in the intended use population
- General study design and objectives have been discussed with FDA:
  - 3 annual test cycles and 2 additional years of follow-up
  - Diagnostic yield
  - Test positivity, PPV
  - Programmatic sensitivity, NPV
  - Compliance to screening with Epi proColon
  - Adherence to diagnostic follow-up after positive Epi proColon
- Detailed protocol to be developed with FDA

# Risk-Benefit Analysis

**David Johnson MD MACG FASGE FACP**

Professor of Internal Medicine

Chief of Gastroenterology

Eastern Virginia Medical School

Norfolk VA

# Risk–Benefit: Potential Risks

- Off-label use
- Minimal procedural risk
- False negative result
- False positive result

# Risk–Benefit: False Negative Result

100,000 subjects 0.7% Prevalence	700 CRC cases		99,300 Non-CRC cases		Missed Cancer	Colonoscopy
	True Positive	False Negative	False Positive	True Negative		
No Screening	NA	NA	NA	NA	700	0
Colonoscopy	700	0	0	99,300	0	100,000
Epi proColon	<b>505</b>	<b>195</b>	19,037	80,263	<b>195</b>	19,542
OC FIT-CHEK	<b>476</b>	<b>224</b>	2,573	96,727	<b>224</b>	3,049

# Risk–Benefit: False Negative Result

- Patient with CRC undetected

## Missed Cancers

- Compared with colonoscopy
  - Non-invasive tests have elevated risk
- Epi proColon compared with OC FIT-CHEK
  - Equivalent nDLR = 0.33
- Relative to OC FIT-CHEK
  - No elevated risk related to negative test result

# Risk–Benefit: False Positive Result

- Positive Epi proColon - CRC negative colonoscopy
- Subsequent colonoscopy due to false positive result
  - Risk of colonoscopy adverse events
    - not attributable to false positive Epi proColon results
  - Large majority of colonoscopy serious adverse events
    - are related to clinically indicated interventions
  - Patients referred to standard of care
    - under colonoscopist's direction

# Risk–Benefit: Overview

## Epi proColon for CRC Screening

- First effective blood test
- Manageable risks
- May increase screening participation
- Blood testing is routine **80% = ACS goal 2018**
- Additional non-invasive test choice

# Closing the GAP!

# **Sponsor: Epigenomics AG**

## **PMA: P130001**

Molecular and Clinical Genetics Panel Meeting  
Medical Devices Advisory Committee

March 26, 2014



# Q&A Responders

## Presenters

Moderator

Dr. Thomas Taapken,  
CEO, Epigenomics

Clinical Practice and  
Non-inferiority Trial

Dr. David Johnson,  
MD. Professor of Internal Medicine and  
Chief of Division of Gastroenterology,  
Eastern Virginia Medical School

Analytics and Pivotal Trial

Dr. Nicholas Potter,  
Ph.D, FACMG, Chief Scientific Officer, Molecular  
Pathology Laboratory Network (MPLN)

## Additional Experts

Clinical Data, Biostatistics

Dr. Gunter Weiss,  
VP Product Development. Epigenomics

Assay Development, Biology

Dr. Uwe Staub,  
COO, Responsible for R&D, Manufacturing,  
Quality. Epigenomics